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Rebates in the Pharmaceutical Industry: Evidence from Medicines Sold in Retail Pharmacies in the U.S.

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ABSTRACT

Rising list prices are often used to illustrate the burden of prescription drug spending, but payers routinely negotiate rebates from manufacturers that generate differences between list and net prices. List prices are easily available and affect patient cost-sharing, but net prices are confidential and affect innovation incentives. We use novel data on medicines sold in a retail setting to quantify rebate growth, the sensitivity of pharmaceutical price indices to list versus net prices, and contribution of net price growth to revenue growth. From 2012 to 2017, we find average rebates increased from 32% to 48%, owing entirely to growth in rebate-levels over a product lifetime rather than shifts towards high rebate products. Annual inflation of list prices was 12% while that of net prices was 3%, implying that financial rewards to manufacturers per unit sold have not grown proportionally to list prices. This pattern is mirrored in 19 of the 20 top drug classes by revenue including insulins, where list and net price inflation were 16% and 2% annually respectively. Finally, we find price growth explains 76% of revenue growth when measured by list prices but 31% of revenue growth when measured by net prices. Moreover, new product entry is the most important factor affecting pharmaceutical revenue growth. These findings provide a cautionary note on using list prices for policy analysis.

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1 Introduction

Pharmaceutical companies are granted market-power through patents and exclusivity periods. The resulting profits increase their incentives to innovate but can strain the ability of patients, payers, and governments to afford these medicines. Rising list prices are often used to illustrate the economic burden of prescription drug prices, but payers, including government payers, routinely negotiate rebates (discounts) from manufacturers that generate differences between list prices and net prices. The confidentiality of rebate data results in researchers and policy-makers relying on list prices or assuming that rebates are fixed or unchanging. For example, several policy and academic reports have have ignored net prices, or assumed that the average rebate is fixed at 5-20% (Health Care Cost Institute, 2017; Gellad et al., 2008). These assumptions are made for convenience but may be incorrect. For example, economic forces such as changes in the relative market power of pharmaceutical firms and purchasers or competition among drugs– via entry and exit– may change rebating over time.

Understanding the level and growth of list prices and prices net of rebates is important for several reasons. First, because pharmaceutical companies receive net prices their incentives to innovate are keyed to these profits using these prices. If list prices are larger than net prices or grow faster, an analyses based on list prices would overstate the dead-weight loss from manufacturers market power and the profits required to induce new innovation. Constructing price indices using list prices would also overstate net price inflation, and thus exaggerate what policy responses like indexing payment to inflation will accomplish. Similarly, analysis of list prices will overstate the contribution of price increases on revenues. Second, pricing dynamics with list prices may be different than those with net prices and relying on the former may cause commentators to believe that more complicated models of imperfect competition– like 'shadow pricing,' where tacit collusion enables an entrant to pick a price higher than an incumbent's– are more central for understanding pharmaceutical pricing dynamics than simpler insights from price-theory (Hartung et al., 2015; Bhattacharya and Vogt, 2003). Third, a divergence between list and net prices can reduce risk-protection for patients because out-of-pocket costs such as coinsurance are often tied to list prices in order to preserve the confidentiality of net prices.[1] Finally, rebates are of interest in their own right for they reflect the relative market power and business models of intermediaries such as pharmacy

[1]For example, in a standard 2020 Medicare Part D prescription drug plan, patients' pay 25% of list prices out-of-pocket after exhausting their deductible and until total spending exceeds the $9719 threshold for catastrophic coverage. Similarly, uninsured patients are typically be responsible for the full list price.

benefit managers (PBMs), which may be changing over time. PBMs are often compensated on the basis of list prices and negotiated rebates, meaning that PBMs may prefer drugs with higher list prices and higher rebates. Unfortunately, little is known about rebate levels and how they have changed over time.

We use data from SSR Health, LLC, a private data aggregator, to shed light on the level and growth of list prices and net prices in the US. SSR Health, LLC aggregates data on U.S. revenue from SEC filings, list prices and US unit sales from Symphony Health, and dosing information from FDA labels. Our sample is composed of branded drugs distributed in traditional retail pharmacies and excludes drugs sold in hospitals or clinics. With data on revenues and quantities, we estimate a net price for each product-formulation and rebates as the difference between list prices and these average net prices (where the average is taken over all US payers). The focus on average net prices received by manufacturers is key for interpreting our results; net prices can vary by market segment (e.g., Medicaid, Medicare, Commercial) and specific payer but we cannot isolate this variation with our data.

Our primary analysis reports changes in average rebates, measured as the ratio between list and net revenues. This ratio has a straightforward interpretation as the percentage reduction in pharmaceutical revenue owed to rebates alone. Overall, we find that pharmaceutical rebates have grown over time, calling into question the practice of assuming fixed rebates over time. We estimate that the average rebate across products increased from 32% to 48% between 2012 and 2017, or 3.2 percentage points per year. We further document that this pattern is relatively consistent across major drug classes. We find that rebates increased for 18 of the 20 largest drug classes by 2017 revenue, ranging from 1.8 to 7.6 p.p. per year.

Next, we note that rebates may grow for two different reasons: substitution towards relatively products with high rebates, through formulary design, or increasing rebate levels within a product. We decompose the change in rebates over time into these drivers using methods have been used to study the firm-level drivers of aggregate productivity growth in traditional sectors such as manufacturing (Foster, Haltiwanger and Krizan, 2001; Foster, Haltiwanger and Syverson, 2008; Baily et al., 1991), and the hospital-level drivers of quality improvement (Chandra et al., 2016). We find that annual growth in rebates is almost fully explained by within-product increases in rebates rather than shifts towards products with larger rebates. If anything, there were shifts into products with lower rebate levels including entry of drugs with lower rebate levels. This would be consistent with drugs in high demand being able to maintain high net prices.

This finding leads us to observing that growing rebates could result either from rising list prices and stagnant net prices or stagnant list prices and falling net prices. We calculate that annual inflation for the medicines in our analysis is 12% when estimated using nominal list prices and 3% when estimated by nominal net prices. This compares to a 1.4% average annual inflation in consumer goods from 2012-2017, as measured by the consumer price index (CPI), and 3.8% annual increase in commercial medical prices across 112 metropolitan areas from 2012 to 2016 (Health Care Cost Institute, 2018).

We use these insights to perform a case study of four drug classes that have routinely attracted considerable policy attention: insulins, GLP-1 agonists for diabetes, direct-acting antivirals for hepatitis C, and combination anti-virals for H.I.V. Much of the public reporting on insulins has focused on rising list prices. We find, however, that rebates for insulins also increased from 39% to 68% from 2012 to 2017. This is due to 16% annual increases in list prices but 2% annual increases in net prices. On the other hand, rebates for hepatitis C anti-virals increased from 4% to 47% from 2014 to 2017 driven by a decline in list and net prices by 1% and 19% per annum respectively. For GLP-1 agonists for diabetes, both list and net prices rose by 22% and 13% per annum from 2012-2017 respectively. Finally, for combination anti-virals for H.I.V, list and net prices grew by 9% and 13% per annum from 2012-2017 respectively, resulting in lower rebate shares.

Finally, we estimate the contribution of rising prices to growth in pharmaceutical revenues. Pharmaceutical revenues are different than drug spending– the former is what is received by manufacturers while the latter includes payments to intermediaries such as wholesalers, PBMs, and retailers. We use net and list prices to impute net and list pharmaceutical revenue and decomposition methods to understand the sources of growth in pharmaceutical revenue. Using net prices, we find that 31% of annual net revenue growth is explained by within-product price growth with the remainder explained primarily by new product entry. The entry of new products is responsible for the overwhelming balance of revenue increases, whereas volume decreases for existing products, holding prices fixed, reduce revenues a lot more than the actual exit of a product. In contrast to these facts, list price increases explain 76% average annual growth in pharmaceutical revenues and would lead commentators to see a tight connection between revenues and list price increases and perhaps infer that list price increases translate into directly into profits because marginal costs are low.

There are other reports suggesting that list prices have grown faster than net prices for branded drugs (The Office of the Inspector General, 2019; IQVIA Institute, 2017; Sood et al.

2020; **?**). The Office of the Inspector General (2019) documents increases in rebates specifically for Medicare Part D, IQVIA Institute (2018) is an industry report suggesting rebate increases over time, and Sood et al. (2020) highlight a correlation between list and net price growth.

Our work is most similar to Hernandez et al. (2020), who also use SSR Health data and a balanced sample of drugs, and estimate that list prices increased by 9.1% while net prices increased by 4.5% annually (similar to our findings on within-product net price increases). We build on Hernandez et al. (2020) in several ways. First, we connect price growth, volume growth, entry and exit to revenue growth. Second, we do not ignore new drugs and our price indices account for new drugs through chain-weighting. We believe that this provides a more accurate measure of inflation than the price increases for products that always existed. Third, we report differential trends in list and net prices of commonly used drugs. Finally, Hernandez et al. (2020) measure average price growth by weighting products based on the number of units sold (i.e., tablets, vials, or injections). This overweights products with small doses and more units relative to their contribution to drug spending. In contrast, we weight products based on their revenue contribution to drug spending, which is a more economically meaningful quantity. There are other differences in sample construction where we believe our choices, detailed in the Appendix, is more robust.

Another related paper is Dafny, Ody and Schmidt (2017) who note that direct-to-consumer rebating in the form of pharmaceutical coupons has increased in recent years, and increases utilization. However, Dafny, Ody and Schmidt (2017) are interested in copayment relief for patients rather than the broader suite of rebates given to wholesalers, pharmacies, and PBMs, which all affect net prices received by manufacturers. Our estimates include both copayment relief and other sources of pharmaceutical rebates.

The remainder of the paper proceeds as follows. Section II describes the data, Section III characterizes the evolution of pharmaceutical rebating, Section IV illustrates differences in economic analyses of price and revenue growth using list versus net prices, and Section V concludes.

2 Data

Our primary data is provided by SSR Health, LLC, a private data aggregation company which provides data on list and estimated net prices for pharmaceutical products. SSR Health, LLC sells access to this data to pharmaceutical companies and investment firms to assist in their

business decisions. The SSR Health, LLC dataset is restricted to branded products[2], which account for the vast share of pharmaceutical spending (Long, 2018). The data excludes unbranded generic products and products sold by private companies. [3] Their data include 1117 branded products encompassing 3271 product-formulations from 2007 onwards. These include data on quarterly revenues in the US by product from SEC filings. While not legally mandated, the industry norm, driven by investor demand, is to report US sales for economically material products. Thus, US revenue data is available for most pharmaceutical products with meaningful sales. SSR Health also purchases data on unit sales and list prices from Symphony Health. Symphony Health is a private data vendor that estimates unit sales using data on prescriptions filled from pharmacies. Units are typically defined as a price per pill / vial / pen / patch. The list price provided by SSR Health, LLC via Symphony Health refers to the Wholesale Acquisition Cost (WAC). Wholesale Acquisition Cost is the unit list price that the pharmacy pays when purchasing medicines from distributors (Dabora, Turaga and Schulman, 2017). Average net prices are then estimated for each product as manufacturer revenue per unit sold. Thus, the average net price per product-formulation refers to the average estimated price received by the manufacturer net of rebates to all parties (e.g., insurers, pharmacy benefit managers, distributors, or patients). The average net price is taken across payers from all segments– Medicare, Medicaid, and commercial. Notably, the average net price is lower than the average cost paid by society, as it is not inclusive of the costs of distribution borne by the distributor and pharmacy or the administrative costs of benefit management borne by the payer.

The data also includes information on U.S. market launch, exit, and loss of exclusivity dates. We classified drugs into therapeutic classes using the hierarchical Anatomical Chemical Therapeutic (ATC) categories, defined by the World Health Organization. Further details on the classification of drugs into ATC categories are provided in the Appendix Section 1.

These data have three noteworthy limitations that we sought to mitigate. First, the unit sales data from Symphony Health may be measured with sampling error. This is especially likely to occur in non-traditional distribution channels such as hospitals, clinics, or specialty pharmacies where Symphony Health's coverage is weaker. Second, data provided by pharmaceutical companies or Symphony Health can be missing for certain products or product-years. This is most likely to occur for smaller products with less commercial significance. Finally, revenue data in quarterly SEC

[2]The data include branded products that have lost exclusive marketing rights but are still sold under the brand name.

[3]Major pharmaceutical companies are typically public, but there are notable exceptions such as Purdue Pharmaceuticals and Boehringer Ingelheim.

fillings is typically recorded earlier than unit sales data from Symphony. Specifically, revenue data is recorded when products are sold to distributors and pharmacies while unit sales data are recorded when prescriptions are filled by patients. This can lead to excess variation in estimates of net prices that are measured in narrow time bins or during new product launches and loss-of-exclusivity when distributors and pharmacies may be building or depleting inventory.

We took several steps to address these limitations. First, we limited our analysis to product formulations on the market at any point between 2012-2017 as the data are more complete during this time period, and SSR Health reports greater accuracy of unit sales data in more recent years. We also focused on 1962 drugs for non-rare diseases likely to be sold in retail pharmacies, which account for $114 Billion in 2017 net US revenue. Specifically, we dropped formulations that were either injectable, oncology products, vaccines, diagnostic compounds, implants or devices, or products approved for an orphan indication by the FDA. [4] [5]. The excluded products accounted for $155.2B in revenue, as shown in Appendix Exhibit 1.

We excluded 1016 disproportionately small product-formulations with missing data for 1 or more years between 2012-2017 despite the product being on the market at the time. These product-formulations accounted for $10.8 Billion in 2017 net US revenue. We also excluded 118 products, accounting for $9.1 Billion in 2017 net US revenue, experiencing loss-of-exclusivity within one year of baseline or endline. We also excluded 32 products, accounting for less than $1 Billion in 2017 net US revenue, that were not linked to ATC categories or with outlier changes in net or list prices during the study period. Finally, we only include a product-years in the analysis if the product is offered for the full year. We report estimates at the annual level to smooth over timing differences in the reporting of revenue and unit sales. Further details on the data limitations, our approach, and our exclusions are provided in the Appendix Section 2.

Our final sample includes 726 total product-formulations. Due to product entry and exit, the sample includes 561 product-formulations in 2012 and 682 product-formulations in 2017. In 2012, the average net revenue associated with each product-formulation was $106 Million, with all product-formulations representing $59.3 Billion in net revenue. In 2017, the mean net revenue asso-

[4] We did not exclude products where the only approved Orphan indication was for a pediatric condition, as this often suggests that the product is used in a broader population in practice. For example, the Hepatitis C product Sovaldi is approved for the Orphan indication of pediatric Hepatitis C despite being used in the broader Hepatitis C population.

[5] The Centers for Medicare and Medicaid (CMS) publishes estimates of average net prices for drugs paid by Medicare Part B, which would include many drugs offered in a hospital outpatient setting, but these numbers exclude Medicaid rebates and so do not represent average net prices received by manufacturers. At the time of writing this paper, Medicaid covered approximately 72 million people

ciated with each product-formulation was $136 Million, with all product-formulations representing $92.9 Billion in net revenue. Additional summary statistics on the final sample can be found in Appendix Exhibits 1 and 2.

3 Evolution of pharmaceutical rebating

3.1 Total growth in rebate share

We first report the size of rebates over the 2012-17 period across the full-sample. We do this by comparing growth in actual pharmaceutical revenue to a counterfactual in which products were sold at list, as opposed to net, prices. The difference between the counterfactual revenue at list prices and actual pharmaceutical revenue represents the rebate share. The rebate share in a given year can be interpreted as the total reduction in pharmaceutical spending due to rebates in this sample, holding quantities in that year constant.

Formally, the total rebate share in year t ($rebate_t$) can be expressed as equation 1. Here, $p_{i,t}^{net}$ reflects the estimated net price for product-formulation i in year t, and S_t represents all products on the market for the full year t.

$$rebate_t = \frac{\sum_{i \in S_t} q_{i,t}(p_{i,t}^{list} - p_{i,t}^{net})}{\sum_{i \in S_t} q_{i,t} p_{i,t}^{list}} \tag{1}$$

The results from these analyses are depicted in Exhibit 1 (Panel A). From 2012-2017 we estimate that the total rebate share increased by 16 p.p. from 32% to 48% of list prices. This corresponds to an annual growth in total rebate shares of 3.2 p.p. To demonstrate the robustness of this result, we assess the sensitivity of these results to several alternatives adjusting our exclusion criteria related to data completeness, loss of exclusivity, and outliers (Appendix Exhibit 3).

3.2 Drivers of of rebate share growth

The growth in rebates over time may be driven by multiple dynamics; changes in rebates could reflect changing rebate levels within product or shifts into products with differing rebate levels. Moreover, market share shifts could happen among products existing in both periods, due to the entry of new products, or due to product exit. To determine the relative contribution of these forces, we first decomposed the rebate change across each pair of adjacent years in our study period (e.g., 2012-2013, 2013-2014, etc.) into four components per equation 2. Notably, performing the decomposition on an annual basis rather than from 2012 to 2017 reduces the component explained

by entry and exit. This is analogous to a chain-weighted approach to calculate quantities such as inflation and GDP growth, which also relies on estimation in narrower temporal categories to reduce the impact of the changing bundle of goods offered.

$$\underbrace{rebate_t - rebate_{t-1}}_{\text{Annual change in avg. rebate}} = \underbrace{\sum_{i \in B_{t,t-1}} \theta_{it-1}(r_{it} - r_{it-1})}_{\text{Within}_{t,t-1}} + \underbrace{\sum_{i \in B_{t,t-1}} (\theta_{it} - \theta_{it-1}) * (r_{it-1} - rebate_{t-1})}_{\text{Between}_{t,t-1}} + \underbrace{\sum_{i \in B_{t,t-1}} (\theta_{it} - \theta_{it-1}) * (r_{it} - r_{it-1})}_{\text{Cross}_{t,t-1}} + \underbrace{\sum_{i \in N_{t,t-1}} \theta_{i,t}(r_{it} - rebate_{t-1})}_{\text{Entry}_{t,t-1}} + \underbrace{\sum_{i \in X_{t,t-1}} \theta_{i,t-1}(rebate_{t-1} - r_{it-1})}_{\text{Exit}_{t,t-1}} \tag{2}$$

$$\theta_{it} = \frac{q_{it} p_{it}^{list}}{\sum_{i \in S_t} q_i t p_{it}^{list}} \tag{3}$$

$$r_{it} = \frac{p_{it}^{list} - p_{it}^{net}}{p_{it}^{list}} \tag{4}$$

The term θ_{it} is defined by equation 3 and refers to market share, measured as the share of list revenue, in year t attributable to product i among the set S_t of all products offered in year t. The term r_{it} is defined in equation 4 and is the share of list price rebated for product i in year t. The term $B_{t,t-1}$ refers to the set of products offered in both periods t and $t-1$, $N_{t,t-1}$ refers to the set of products offered in year t but not year $t-1$, and $X_{t,t-1}$ refers to the set of products offered in year $t-1$ but not year t. Finally $rebate_t$ is defined as in equation 1 and refers to the average rebate in year t.

Thus, in equation 2, the $within_{t,t-1}$ term is the component of rebate growth from year $t-1$ to t that is fully explained by growth in the rebate for each product-formulation, assuming market shares do not change. Meanwhile, the $between_{t,t-1}, cross_{t,t-1}, entry_{t,t-1},$ and $exit_{t,t-1}$ terms together comprise the component of rebate growth from year $t-1$ to t attributable to market share increases among product-formulations with higher rebates. Specifically, $between_{t,t-1}$ is the component attributable to increasing market share among product-formulations that already had relatively high rebates in period $t-1$, $cross_{t,t-1}$ is the component attributable to increasing

market share among product-formulations with growing rebate shares, $entry_{t,t-1}$ is the component attributable to the entry of relatively high rebate products in period t, and $exit_{t,t-1}$ is the component attributable to the exit of relatively low rebate products in period t. These terms will be negative if the forces that they measure move in opposite directions to overall rebate growth.

The results of this analysis are in Exhibit 1 (Panel B). Growth in average market-wide rebate shares is entirely explained by growth in rebates within products over time. Market share shifts have actually tended towards products with lower rebates. This is consistent with products in high demand being able to negotiate higher net prices. If there were no shift in market share across products, including no product entry or exit, then rebates would have increased 4.8 p.p. per year rather than 3.2 p.p. per year on average. Conversely, shifts in market share towards product-formulations with lower rebates reduced rebate growth by 1.6 p.p. per year on average.

3.3 Rebate trends by drug class

We investigated heterogeneity in rebate share growth in the largest 20 drug classes by total net revenue. We focused this analysis on the narrowest grouping of drugs available (ATC-level4 class) as these drugs could reasonably be considered imperfect substitutes.[6] In 2012, this sample of 20 drug classes accounted for 30% (169) of the product-formulations and 58% ($34.2 Billion) of net revenue in study sample. Similarly, in 2017, these drug classes accounted for 31% (213) of the product-formulations and 59% ($54.6 Billion) of net revenue in our study sample. For each drug class, we estimated rebate shares from 2012-2017 using equation 1. We then decomposed rebate share growth into components related to within product rebate growth and market share shifts towards products with differing rebate levels, per equation 2. Appendix Section 4 provides more detail on the selection of classes for this analysis.

The results from this analysis are in Exhibit 2. There is heterogeneity across classes in rebate growth, but almost all classes considered experienced growth in rebates. 18 of the 20 drug classes depicted saw increases in rebate shares, ranging from 1.8 p.p. to 7.6 p.p. per year. The only classes to see a reduction in rebates were combinations of direct-acting anti-virals for H.I.V., where rebates decreased by 1.4 p.p. per year, and proton pump inhibitors for peptic ulcers

[6] We excluded from consideration any classes capturing a miscellaneous assortment of drugs within an ATC-level3 class. As an example, we exclude the ATC-level 4 class J01XX, which captures "other antibacterials for systemic use". This includes all antibacterials that are not defined by another ATC-level4 class. We also exclude classes defined by a broad mechanism of action, in which specific products are not close substitutes. As an example, we exclude the ATC-level4 category L04AA which captures selective immunosuppressive drugs. This includes drugs like Cellcept, which prevents organ rejection after transplant, and orencia, which is for auto-immune diseases like rheumatoid arthritis.

and gastroesophageal reflux disease, where rebates decreased by 1.2 p.p. per year. Consistent with our earlier results, for all the drug classes experiencing rebate growth, the within-product average annual rebate growth was fully or near-fully explained by increases in rebate growth within product, rather than shifts towards products with larger rebates. However, there is heterogeneity across classes on the role of market share shifts: in 9 out of the 18 classes in which rebates grew, market share shifts actually pushed towards product-formulations that reduced rebate growth.

4 Contrasting economic analyses of net and list prices

The level of pharmaceutical rebates and changes in rebating over time imply that analyses of pharmaceutical pricing will yield different results depending on whether net or list prices are used. In this section we illustrate this point by demonstrating differences in price indices overall and by drug class and in the contribution of price increases to estimates of total pharmaceutical revenue growth.

4.1 Estimates of pharmaceutical price inflation

4.1.1 Laspreyres price inflation

We estimated list and net price growth per treatment course, or for an annual supply when a standard treatment course was not defined. This exercise is richer than the simply focusing on rebates, because increasing rebates, as illustrated in Exhibit 2, could be consistent with increasing, flat, or decreasing net prices so long as list prices grew faster or did not decline as quickly. This exercise also allows us to highlight the dollar value of divergence between list and net prices.

We estimate a pharmaceutical price inflation index by measuring inflation from $t-1$ to t using a Laspreyres inflation index estimated on the basis of products available in both periods $t-1$ and t. We then estimate a chain-weighted or compound annual inflation rate by multiplying the Laspreyres inflation indexed for each year-pair from 2012-2017.

Formally, we apply equation 5 to estimate a Laspreyres inflation index between years $t-1$ and t using prices for the set of products appearing in both $t-1$ and t. Here, $g^{list}_{t-1,t}$ and $g^{net}_{t-1,t}$ refer to the estimated price inflation between years $t-1$ and t, calculated using list price and net price, $p^{list}_{i,t}$ and $p^{net}_{i,t}$ refer to prices for product-formulation i in year t, $q_{i,t}$ and refers to unit sales, and $B_{t,t-1}$ is the set of product-formulations offered in both years t and $t-1$.

$$g^{c}_{t-1,t} = \frac{\sum i \in B_{t-1,t}(p^{c}_{i,t} - p^{c}_{i,t-1})q_{i,t-1}}{\sum i \in B_{t-1,t}(p^{c}_{i,t-1}q_{i,t-1})}, c \in (list, net) \tag{5}$$

We then calculate a compound annual inflation rate, $g_{2012,2017}$ by applying equation 6.

$$g_{2012,2017} = \left(\prod_{t \in [2013,2017]} g_{t-1,t} + 1 \right)^{1/5} - 1 \tag{6}$$

Exhibit 3 includes details on the annual Laspreyes inflation indices estimates underlying the compound annual inflation rate by drug class and across all drug classes. We find that estimation with list prices yields a compound annual inflation rate of 12% while estimation with net prices yields a compound annual inflation rate of 3%. This illustrates that financial rewards to pharmaceutical firms per unit sold has not grown in proportion to list price increases. This compares to a 1.4% average annual inflation in consumer goods from 2012-2017, as measured by the consumer price index (CPI), and 3.8% annual increase in commercial medical prices across 112 metropolitan areas from 2012 to 2016 (Health Care Cost Institute, 2018).

We also estimate annual inflation estimates separately for the 20 largest ATC-level 4 drug classes as estimated by total revenue in the study period. While there is some heterogeneity across drug classes, list price inflation was greater than net price inflation for 19 of 20 drug classes. To benchmark these results to the CPI, we find that 13 of the 20 largest ATC-level 4 drug classes experienced net price inflation higher than price inflation for consumer goods, but all 20 experienced list price inflation that exceeded CPI. We emphasize that the comparison to CPI is only for benchmarking purposes; there is no reason to believe that prices should growth at CPI.

These estimates of price inflation have limitations that are shared by all price indices of the type that we have constructed. Our estimates measure inflation on a fixed bundle of goods available in both years of each year-pair and understate inflation because we do not capture higher prices among entering products in the year they enter. We did not control for the quality of new drugs, so if newer drugs are better then our estimates overstate inflation. Moreover, our estimates also overstate the inflationary burden on consumers because we do not have data on generics– the entry of generics causes substitution towards generics because of lower prices; these lower prices are not observed.

4.1.2 Growth in the average cost per therapeutic regimen

We also estimated an alternative price inflation measure, the average price per therapeutic regimen, for the 20 largest ATC-level 4 drug classes. This alternative measure is informative beyond the Laspreyres inflation index for two main reasons. First, it allows us to quantify the magnitude of price increases on spending in dollar terms. Second, it allows us to account for product entry and exit from year-to-year.

To illustrate our approach transparently, we first perform this analysis on a subset of the ATC-level 4 drug classes presented in Exhibit 2 for which SSR Health, LLC collected information on dosing for at least 5 product-formulations between 2012 and 2017. We create an index of the average price per treatment course or annual supply within the class. We do this by weighting product-formulations within a sub-category based the product-formulation's market share of treatment courses or annual supplies sold that year. This provides a simple interpretation for the average price within a drug class in a given year; it is the average price paid by a patient that year for a course or annual supply of a therapy within the drug class.

Exhibit 4 summarizes the trends in list and net pricing for four drug categories: insulins, GLP-1 agonists for diabetes, direct-acting antivirals for hepatitis C, and combination anti-virals for H.I.V. In addition to being of policy interest, these four categories highlight how classes can differ in the evolution of net and list prices, even in cases where rebate share is increasing. In the case of insulins, list prices grew 16% per annum while net prices remained relatively flat, growing at 2% per annum. Among, GLP-1 analogues for diabetes saw increases in both prices, but list prices grew faster (22% per annum) than net prices (13%). Meanwhile, list and net prices for HCV anti-virals increased from 2012-2014 on average by 62% and 88% per annum respectively. This is attributable to Sovaldi, a product considered much more highly effective than predecessors and priced accordingly. However, from 2014 to 2017, net prices decreased 19% per annum while list prices remained stable (1% per annum decrease). This coincides with the entry of additional new-generation HCV therapies (e.g., daklinza, harvoni, epclusa, viekira / XR, zepatier). Finally, H.I.V products saw almost equal growth in list and net prices (9% vs. 11% per annum).

Finally, we quantified the mechanisms underlying changes in average prices per therapeutic regimen. As in the case of rebates and revenue, there are several reasons why average prices may change from year-to-year including increases in the price of products available in both years or shifts to more expensive products. Shifts towards more expensive products may be due to shifts

towards more expensive products already on the market, the entry of higher cost products, or exit of lower cost products. We sought to disentangle the contribution of these forces by decomposing the change in average price per therapeutic regimen using an approach similar to the decompositions of rebate growth in section 3.2. We then compared how the results of this analysis differ depending on whether we use list or net prices.

We do this by first defining η_{ikt}, which refers to product i's share of all therapeutic regimens sold within class k in year t, per equation 7. Here x_{ikt} refers to the the number of therapeutic regimens of product-formulation i in drug class k sold in in period t and S_t^k refers to the set of all products available in period t. A therapeutic regimen may be defined as either the a one-time treatment course or an annual supply, depending on the class.

$$\eta_{ikt} = \frac{x_{ikt}}{\sum_{i \in S_t^k} x_{ikt}} \tag{7}$$

We then define the average price per therapeutic regimen within a drug class k in year t using list and net prices per equation 8. Here, p_{ikt}^{list} and p_{ikt}^{net} refer to the list and net price for product-formulation i in drug class k in year t, $S_{t,t-1}^k$ refers to the set of all products in class k that are offered in at least one year between $t-1$ and t, and, again, η_{ikt} refers to product i's share of all therapeutic regimens sold within class k in year t.

$$\bar{p}_{k,t-1}^c = \sum_{i \in S_{t,t-1}^k} p_{ikt}^c * \eta_{ikt}, c \in list, net \tag{8}$$

We finally decompose the annual growth in price per therapeutic regimens into five components by applying equation 9. Again, $\bar{p}_{k,t}^{list}$ and $\bar{p}_{k,t}^{net}$ are the average price per therapeutic regimen in drug class k in year t as estimated by list and net prices, p_{ikt}^{list} and p_{ikt}^{net} are the list and net price per therapeutic regimen for product-formulation i in drug class k in year t, η_{ikt} is the market share of drug formulation i in class k in year t, $B_{t,t-1}^k$ is the set of product-formulations in drug class k that are available in both years, $N_{t,t-1}^k$ is the set of product-formulations in drug class k that are available in year t and not $t-1$, and $X_{t,t-1}^k$ is the set of product-formulations in drug class k available in year $t-1$ but not year t.

$$\underbrace{\bar{p}^c_{k,t} - \bar{p}^c_{k,t-1}}_{\text{Avg. growth in price per course}} = \underbrace{\sum_{i \in B^k_{t,t-1}} \eta_{ik,t-1}(p^c_{ikt} - p^c_{ik,t-1})}_{\text{Within}^k_{t,t-1}} + \underbrace{\sum_{i \in B^k_{t,t-1}} (\eta_{ikt} - \eta_{ik,t-1})(p^c_{ik,t-1} - \bar{p}^c_{k,t-1})}_{\text{Between}^k_{t,t-1}}$$
$$+ \underbrace{\sum_{i \in B^k_{t,t-1}} (\eta_{ikt} - \eta_{ik,t-1}) * (p^c_{ikt} - p^c_{ik,t-1})}_{\text{Cross}^k_{t,t-1}} + \underbrace{\sum_{i \in N^k_{t,t-1}} \eta_{ikt}(p^c_{ikt} - \bar{p}^c_{k,t-1})}_{\text{Entry}^k_{t,t-1}}$$
$$+ \underbrace{\sum_{i \in X^k_{t,t-1}} \eta_{ik,t-1}(\bar{p}^c_{k,t-1} - p^c_{ik,t-1}), c \in (list, net)}_{\text{Exit}^k_{t,t-1}} \tag{9}$$

Intuitively, we decompose growth in average prices per therapeutic regimen into components that reflect the contribution of increases in the price of existing products versus shifts towards more expensive products. Specifically, the *within* terms are the component of annual increases in the average price per therapeutic regimen increases that is fully explained by growth in the average price for each product-formulation, assuming market share does not change. Meanwhile, the *between, cross, entry,* and *exit* terms together comprise the components of growth in average prices per therapeutic regimen attributable to market share increases among product-formulations with higher prices. Specifically, the *between* terms are the components attributable to increasing market share among formulations that already had relatively high prices per therapeutic regimen in period $t-1$, the *cross* terms are the components attributable to increasing market share among product-formulations with growing prices, the *entry* terms are the components attributable to the entry of relatively high price products in period t, and the *exit* terms are the components attributable to the exit of relatively low price products in period t. Again, these terms can also be negative if these forces detract from growth in average prices per therapeutic regimen

Exhibit 5 illustrates the results of this decomposition for insulins, GLP-1 agonists for diabetes, direct-acting antivirals for hepatitis C, and combination anti-virals for H.I.V. It shows that within product price increases, market share shifts towards lower price product-formulations, and entry of new products all can play an important role in explaining increases in the average price per therapeutic regimen with considerable heterogeneity across drug classes. For example, when estimated using list prices, within product price increases explain 98% of increase in prices per therapeutic regimen for insulins but only 27% of increases in prices per therapeutic regimen

for Hepatitis C anti-virals. This is because the majority of price increases for Hepatitis C anti-virals was driven by shifts from older to newer generation medications with greater efficacy. This heterogeneity persists both when analyzed with list and net prices. For Hepatitis C anti-virals, the contribution of net price changes to increases in the average net price per therapeutic regimen is actually negative. This reflects decreasing net prices among product-formulations on the market, in most years.

4.2 Pharmaceutical revenue growth and the contribution of price growth

Given the popular concern that growth in pharmaceutical revenues is driven considerably by price increases rather than increasing use or innovation (e.g., Hernandez et al. (2019)), we sought to quantify the degree to which annual growth in pharmaceutical revenue can be explained by growth in prices for products already on the market versus changes in the quantity of product used, entry of new products, and the exit of existing products. We then compared how the results of this analysis differ depending on whether we use list or net prices.

We used a decomposition approach similar to the decompositions of rebate and price growth presented in sections 3.2 and 4.1.2. Here, $p_{i,t}^{list}$ and $p_{i,t}^{net}$ refer list and net price per unit for product-formulation i in year t, $q_{i,t}$ and refers to unit sales, $S_{t,t-1}$ is the set of product-formulations offered in at least one year between years $t-1$ and t, $B_{t,t-1}$ is the set of product-formulations offered in both years t and $t-1$, $N_{t,t-1}$ is the set of product-formulations offered in year t but not $t-1$, and $X_{t,t-1}$ is the set of product-formulations offered in year $t-1$ but not t.

$$\begin{aligned}\underbrace{\sum_{i\in S_{t,t-1}} p_{i,t}^{c} q_{i,t} - \sum_{i\in S_{t,t-1}} p_{i,t-1}^{c} q_{i,t-1}}_{\text{Growth in revenue}} = & \underbrace{\sum_{i\in B_{t,t-1}} q_{i,t-1}(p_{i,t}^{c} - p_{i,t-1}^{c})}_{\text{Within}_{t,t-1}} + \underbrace{\sum_{i\in B_{t,t-1}} (q_{i,t} - q_{i,t-1}) p_{i,t-1}}_{\text{Between}_{t,t-1}} \\ & + \underbrace{\sum_{i\in B_{t,t-1}} (q_{i,t} - q_{i,t-1}) * (p_{i,t}^{c} - p_{i,t}^{c})}_{\text{Cross}_{t,t-1}} + \underbrace{\sum_{i\in N_{t,t-1}} q_{i,t} p_{i,t}^{c}}_{\text{Entry}_{t,t-1}} \\ & + \underbrace{\sum_{i\in X_{t,t-1}} -q_{i,t-1} p_{i,t-1}^{c}}_{\text{Exit}_{t,t-1}}, \;\; c \in (list, net)\end{aligned} \tag{10}$$

Equation 10 decomposes growth in drug revenues across all drugs into several components using an approach that is analagous to the approaches used in sections 3.2 and 4.1.2. The *within*

term captures the annual growth in drug revenue explained exclusively by price increases in products available in both years, assuming quantities consumed do not change. The *between, cross, entry,* and *exit* terms therefore collectively capture the degree to which revenue growth is explained by changes in quantities. Specifically the *between* term captures the component of drug spending growth due to increases in quantity (volume) among products available in both periods (while prices are fixed). The *cross* term captures the component of revenue growth due to increases in the quantity for the product-formulations for which prices also increased. Finally, the *entry* term reflects gained revenue from new products and *exit* term reflects lost revenue from exiting products. Assuming entering and exiting products have non-zero sales in the years they are available, the *entry* term will be positive and the *exit* term will be negative. The *within, between,* and *cross* terms may be positive or negative depending on whether they contribute or detract from growth in revenues.

Finally, we determined the average annual contribution of each component in equation 10 to annual drug revenue growth over the full study period using an approach resembling our analysis of rebate share growth in section 3.2. For each term, this was computed by simply adding the annual components from each year-pair from 2012-2013 to 2016-2017 and dividing by the total change in rebates from 2012-2017. For example, to estimate the average share of annual revenue growth accounted for by within-product rebate growth ($Within\ share_{2012,2017}$), we apply equation 11.

$$Within\ share_{2012,2017} = \frac{\sum_{t\in[2013,2017]} within_{t,t-1}}{\sum_{i\in S_{t-1,t}} p^c_{i,t} q_{i,t} - \sum_{i\in S_{t-1,t}} p^c_{i,t-1} q_{i,t-1}} \tag{11}$$

Our results, depicted in Exhibit 6, show that within product price increases (*within term*) play a smaller role in explaining revenues increases when estimated using net rather than list prices. Using net prices, 31% of average annual pharmaceutical revenue growth is explained by growth in prices for products available in both years (*within term*). As a benchmark, if this price growth had mirrored CPI inflation then this percentage would be 18% . The remaining 69% of revenue growth that is not explained by price growth is explained primarily by new product entry (*entry term*), while volume decreases of existing products, holding prices fixed contribute negatively to revenue growth (*between term*). The negative association between price effects and volume effects should not be interpreted to mean that we have estimated a demand curve, but that equilibrium price increases and volume decreases are happening at the same time. The *exit term* is small in

magnitude meaning that product exit per se is not a meaningful driver of manufacturers revenues, relative to the direct effect of losing volume on an existing product.

In contrast, using list prices, we would estimate that that 76% of average annual pharmaceutical revenue growth is explained by growth in prices for products available in both years (*within term*). These differences have large implications for how we view the sources of revenue growth for manufacturers: using net prices instead of list prices for the calculation of revenues halves the contribution of price increases to revenue growth; new product entry is the most important source of revenue growth, and volume decreases of existing products reduce pharmaceutical revenue.

5 Conclusion

We used data on pharmaceutical products sold via retail pharmacy for non-rare diseases to illustrate how our understanding of pharmaceutical price inflation is meaningfully impacted by one's use of list versus net prices. Over the 2012-17 period, pharmaceutical price inflation was 12% per year using list prices but only 3% per year using net prices. We also show that average rebate for increased from 32% to 48% over the same period. We also document heterogeneity in these rebate trends by drug class. Our results also challenge the conventional narrative around the magnitude of price increases for the same drug. We find that price growth for already marketed products explains 76% of annual drug spending growth when measured by list prices but explains a third 31% of annual drug spending growth when measured by net prices. Meanwhile, analyzing net prices reveals that new product entry explains the bulk of revenue growth. Taken together, these results suggest that new product entry is the most important factor driving growth in pharmaceutical revenue. Furthermore, analysts and economists working in public policy should be extremely cautious in drawing policy conclusions based on list prices alone. If nothing else, the focus on net prices would reduce the reliance on more complicated models of imperfect competition– like 'shadow pricing'– over simpler insights from price-theory (Hartung et al., 2015; Bhattacharya and Vogt, 2003).

The divergence between list and net prices has uncertain welfare effects. On the one hand, this trend implies that the total cost of medicines to payers has not increased as dramatically as trends in list prices would suggest. These savings are partially passed to consumers or taxpayers in the form of lower plan premiums. However, if there is imperfect competition among PBMs or insurers, part of these savings are likely to be retained by PBMs or insurers (Dafny, Duggan and Ramanarayanan, 2012; Ho and Lee, 2017). To the extent that savings are being retained as profit

by intermediaries who are not responsible for innovation, they reduce incentives for innovation without improving affordability. For all these reasons, our analysis does not reveal whether net prices are higher or lower than the social optimum.

On the other hand, because patients' out-of-pocket costs are often pegged to list prices, growing list prices mean that patients are paying for an increasing share of pharmaceutical spending through out-of-pocket payments. We can perform a simple calculation to benchmark this phenomena. For example, our results suggest that, for fast-acting insulins from 2012-2017, revenue based on list prices grew from \$5.3 to \$13.2 Billion while net revenue only grew from \$2.9 to \$3.5 Billion. This implies that if a diabetic patient in a standard Medicare Part D plan and between his or her deductible and the catastrophic coverage threshold is purchasing a fast-acting insulin, then his or her out-of-pocket payment (25% of list price) would have accounted for 37% of pharmaceutical revenue under 2012 list prices and rebate shares and 75% of pharmaceutical revenue under 2017 list prices and rebate shares. Thus, while insured patients with fewer health needs may benefit from lower premiums associated with rebates, sicker or uninsured patients may be worse off and may forgo valuable drugs (Herkert et al., 2019). As a result, growing rebates may be regressive and may have reduced the financial protection from insurance. We underscore that this is just an illustrative calculation, and heterogeneity in prescription drug plans and the non-linearity of insurance contracts makes it difficult to precisely estimate the share of total pharmaceutical revenue accounted for by out-of-pocket payments.

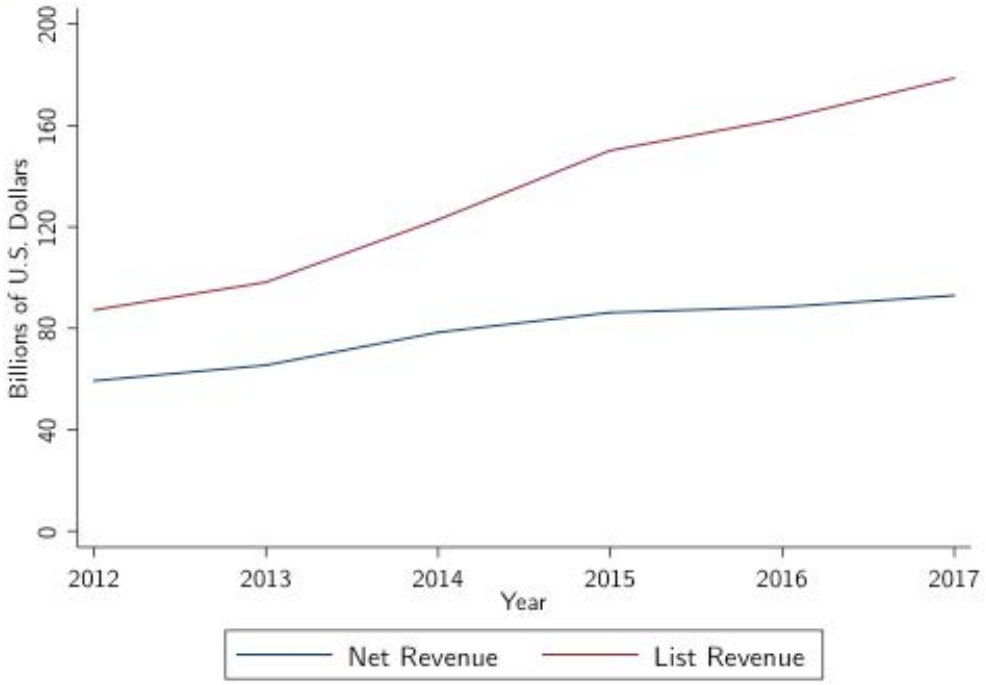
There are noteworthy caveats to our analysis. Our results may not generalize to a broader set of products including biologic drugs those provided in hospitals, clinics, or for rare-diseases; it is possible that market structure for these drugs is different. Second, because of using chain-weighted indices, our estimates of price inflation does not consider the price of new products in their year of entry, which understates inflation. Pushing in the other direction, our estimates will overstate inflation experienced by patients because products go generic and we lack data on the prices of generics. Third, we are unable to adjust for the quality of new drugs and this will cause us to overstate inflation if newer drugs are better. Finally, we cannot segment trends by payer markets, which differ substantially in rebating behavior. As a result our analysis does not translate easily to policy simulations involving specific payer-segments such as Part D, Medicaid, or commercial insurance.

Our analysis rules out simple substitution towards higher rebate products, but cannot uncover the mechanism underlying faster growth in list than net prices, or the sources of heterogeneity

across drug classes. This limitation reflects our design– we do not observe exogenous changes to competition. This should be an active area for other work and there are several hypotheses worth exploring. First, it is possible that because PBMs are compensated based on a combination of list prices and negotiated rebates, PBMs prefer products with higher list prices and higher rebates thus increasing rebating behavior over time. Second, it is possible that increasing competition within drug class reduces net prices over time. One example of this may be HCV anti-virals, where net price decreases coincided with the release of multiple new treatments were released from 2013 onwards. Competition from new branded products may be partially responsible for decreases in net prices for HCV products from 2014-2017, where new product entry may have allowed payers to demand larger rebates by creating more options for formulary design. While prior work has found limited impact of competition on list prices (see Sarpatwari et al. (2019)), our findings highlight the importance of studying the effect of competition on net prices. Third, it is possible that, increasing market power by purchasers (e.g., PBMs, insurers, distributors) may increase negotiated rebates. Finally, it is possible that rebate increases are due to increases in the share of pharmaceutical spending done via government programs mandating rebates such as Medicaid and the 340B Program. For example, rebates for H.I.V. declined modestly from 2012-2017. One hypothesis is that this may reflect Medicaid coverage for a disproportionate share (42%) of all H.I.V. patients, so it is possible that Medicaid rules concerning mandatory rebates may prevent a large divergence between list and net prices for this drug class. Disentangling these explanations for rebate growth is worthy grounds for future research.

Exhibit 1: Pharmaceutical rebate growth (2012-2017)

Panel A: Annual Rebate Growth



Year	2012	2013	2014	2015	2016	2017	Avg. Annual Growth
Net Rebates (%)	32%	33%	36%	43%	46%	48%	3.2 p.p.
Sample (N)	561	571	589	614	654	682	

Panel B: Sources of Rebate Growth

Year	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017	Avg. Annual Growth
Rebate Change (p.p.)	1.3	2.8	6.4	3.0	2.4	3.2
Sources of Rebate Growth						
Within	1.7	5.8	7.2	5.1	4.3	4.8
Between	-0.6	-0.8	0.5	-0.8	-1.0	-0.5
Cross	0.3	0.0	-1.7	-0.7	-0.2	-0.5
Entry	-0.2	-2.2	0.5	-0.5	-0.8	-0.6
Exit	0.2	0.0	0.0	0.0	0.0	0.0
Sample (N)	583	604	616	659	692	

Notes: In Panel A, rebate shares are calculated based on the ratio of revenue estimated by list prices and net prices for 726 branded product-formulations sold in retail pharmacies for non-rare conditions. Samples differ by year due to product entry and exit. See text for further details on exclusions. Panel B reflects decomposes the annual growth in rebate levels into five components corresponding to distinct mechanisms contributing to rebate growth. The *within* term is the component of rebate growth that is fully explained by growth in the rebate for each product-formulation, assuming market share does not change. The *between*, *cross*, *entry*, and *exit* terms together comprise the component of rebate growth attributable to market share increases among product-formulations with higher rebates. The *between* term is the component of rebate growth attributable to increasing market share among product-formulations that already had relatively high rebates in the baseline year, The *cross term* is the component of rebate growth attributable to increasing market share among product-formulations with growing rebate shares. The *entry* term is the component of rebate growth attributable to the entry of relatively high rebate products in the endline year. Finally, the *exit* term is the component of rebate growth attributable to the exit of relatively low rebate products in the endline year. These terms are negative when the forces that they measure move in opposite directions to overall rebate growth. Equation (2) in the main text expresses this decomposition mathematically.

Exhibit 2. Sources of Rebate Growth for the 20 Largest Drug Categories

Disease or use case	ATC-4 category	2012			2017			Avg. annual rebate growth	Sources of rebate growth (p.p.)				
		Rev. ($B)	Rebate (%)	Drugs (N)	Rev. ($B)	Rebate (%)	Drugs (N)		Within	Between	Cross	Entry	Exit
Peptic ulcers or gastro-oesophageal reflux disease	Proton pump inhibitors	2.9	64%	16	1.1	57%	16	-1.2 p.p.	-0.54	-1.87	1.16	0.00	0.00
Ulcerative colitis	Aminosalicylic acid and similar agents	0.7	18%	3	0.4	44%	3	5.2 p.p.	5.32	1.58	-2.40	0.27	0.48
Exocrine pancreating insufficiency	Digestive enzyme preparations	0.5	17%	10	0.7	29%	12	2.5 p.p.	2.41	0.03	0.02	0.01	0.00
Diabetes	Insulins, fast-acting	2.9	45%	11	3.5	73%	11	5.6 p.p.	5.38	0.06	0.15	0.00	0.00
Diabetes	Insulins, intermediate- or long-acting combined with fast-acting	1.0	47%	11	0.8	71%	11	4.8 p.p.	4.51	0.08	0.20	0.00	0.00
Diabetes	Insulins, long-acting	4.8	29%	4	5.9	63%	10	6.8 p.p.	7.39	-0.28	-0.08	-0.26	0.00
Diabetes	Combinations of oral blood glucose lowering drugs	1.0	27%	8	1.3	65%	21	7.6 p.p.	7.48	0.05	-0.12	0.20	0.00
Diabetes	Deipeptidyl peptidase 4 (DPP-4) inhibitors	2.6	27%	6	2.9	64%	6	7.3 p.p.	7.11	0.09	0.12	0.00	0.00
Diabetes	Glucagon-like peptide-1 (GLP-1) analogues	1.4	11%	3	4.8	38%	9	5.5 p.p.	5.51	-0.32	-0.07	0.39	0.00
Preventing or treating blood clots	Direct factor Xa inhibitors	0.2	7%	3	5.4	43%	8	7.3 p.p.	7.35	0.03	-0.15	0.02	0.00
Contraception	Progestogens & estrogens in combination	0.8	26%	13	0.6	35%	12	1.8 p.p.	3.15	-0.63	-0.15	-0.29	-0.01
Male hypogonadism	3-oxoandrosten (4) derivatives androgens	1.3	27%	9	0.7	50%	9	4.7 p.p.	4.62	-0.02	0.06	0.00	0.00
Menopause	Estrogen treatment	1.0	19%	21	0.9	35%	20	3.2 p.p.	3.23	0.01	0.00	0.00	0.00
Incontinence	Drugs for urinary frequency	0.8	40%	8	1.1	58%	10	3.4 p.p.	4.19	-0.75	0.31	-0.32	0.00
Hepatitis C	Direct-acting antivirals	0.3	29%	1	6.5	47%	8	3.7 p.p.	20.18	0.60	-12.24	-5.42	0.00
HIV	Combinations of direct-acting antivirals	4.1	36%	3	11.8	29%	8	-1.4 p.p.	0.24	-0.84	0.11	-0.71	0.00
Various	Selective serotonin (5HT1) agonists	0.3	10%	12	0.2	34%	12	4.8 p.p.	2.70	1.49	0.64	0.00	0.00
Obstructive Airway Diseases	Selective beta-2-adrenoreceptor agonists	1.1	51%	6	1.3	64%	4	2.7 p.p.	2.58	-0.47	0.34	0.00	0.03
Obstructive Airway Diseases	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics	5.2	33%	10	3.5	67%	10	6.7 p.p.	4.83	-0.08	0.00	0.00	0.00
Obstructive Airway Diseases	Glucocorticoids	1.0	45%	11	1.2	69%	13	4.8 p.p.	2.84	0.86	0.02	-0.19	0.00

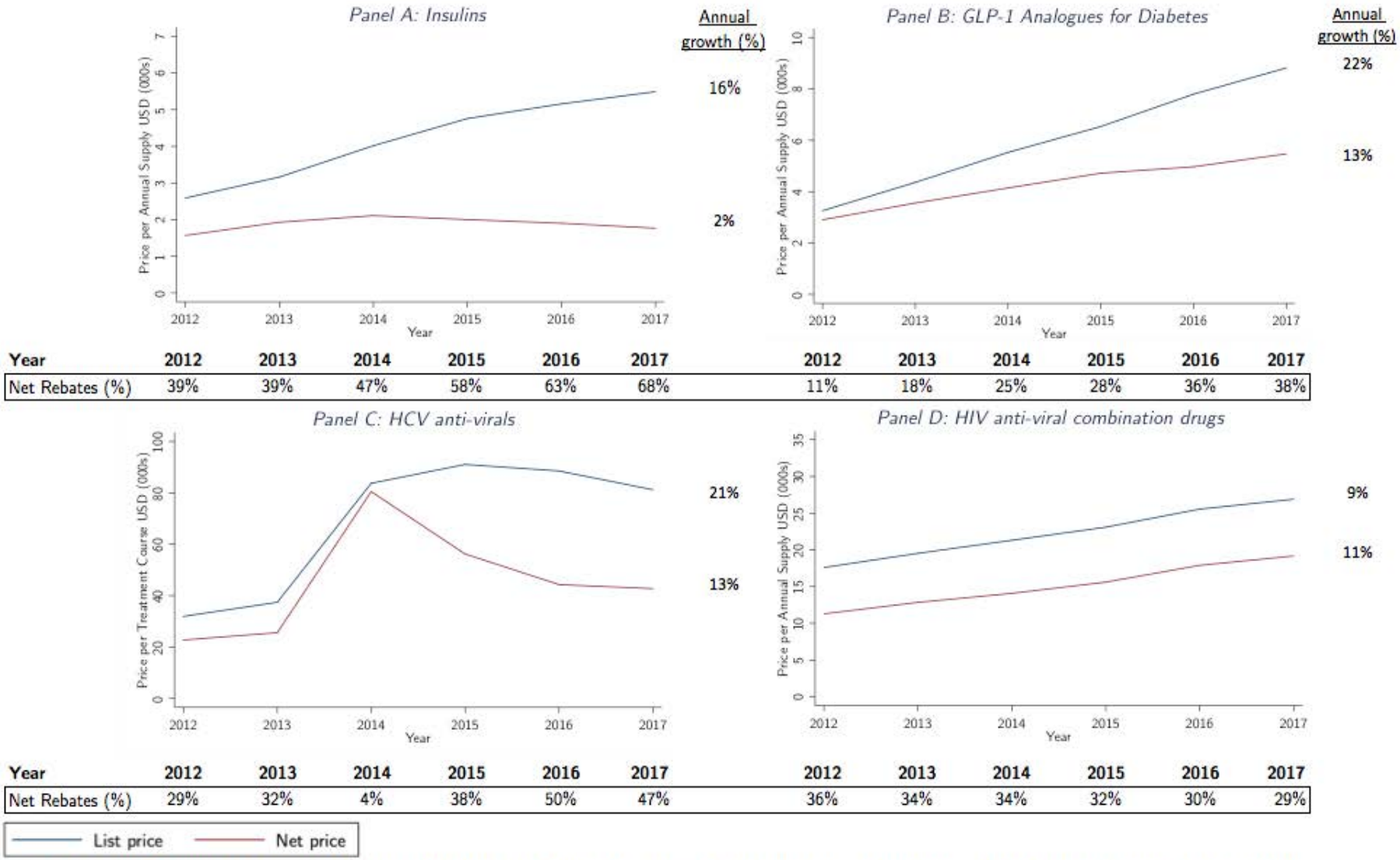
Note: ATC-level 4 categories are the narrowest drug category defined by the World Health Organization Collaborating Centres (WHOCC). The drugs in these categories thus typically reflect relatively close, but imperfect, clinical substitutes. This figure includes the 20 ATC-level 4 drug classes with the highest total revenue between 2012-2017. We exclude from this analysis ATC-level 4 categories in which we observe fewer than 5 product-formulations between 2012-2017 or ATC-level 4 categories that reflect a miscellaneous assortment of products, as these may not be close substitutes. For example, we exclude the ATC-level 4 class J01XX, which captures "other antibacterials for systemic use". Drug counts represent number of product-formulations. In each ATC-level 4 category and year, rebate shares are calculated based on the ratio of revenue estimated by list prices and net prices. The average annual change in the rebate share from 2012 to 2017 in each ATC-level 4 category is then decomposed into five components corresponding to distinct mechanisms contributing to rebate growth. The *within* term is the component of rebate growth that is fully explained by growth in the rebate for each product-formulation, assuming market share does not change. The *between*, *cross*, *entry*, and *exit* terms together comprise the component of rebate growth attributable to market share increases among product-formulations with higher rebates. The *between* term is the component of rebate growth attributable to increasing market share among product-formulations that already had relatively high rebates in the baseline year, The *cross* term is the component of rebate growth attributable to increasing market share among product-formulations with growing rebate shares. The *entry* term is the component of rebate growth attributable to the entry of relatively high rebate products in the endline year. Finally, the *exit* term is the component attributable to the exit of relatively low rebate products in the endline year. These terms are negative when the forces that they measure move in opposite directions to overall rebate growth. Equation (2) in the main text expresses this decomposition mathematically.

Exhibit 3. Pharmaceutical price inflation (2012-2017)

		List price inflation						Net price inflation						Balanced sample (N)				
		2012-2013	2013-2014	2014-2015	2015-2016	2016-2017	Avg. Annual	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017	Avg. Annual	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017
Overall		14%	16%	13%	9%	7%	12%	11%	6%	0%	0%	-1%	3%	549	556	587	609	644
Disease Area	**ATC-4 category description**																	
Peptic ulcers or gastro-oesophageal reflux disease	Proton pump inhibitors	14%	13%	6%	5%	3%	8%	3%	6%	-15%	14%	47%	9%	16	16	16	16	16
Ulcerative colitis	Aminosalicylic acid and similar agents	13%	11%	16%	9%	8%	11%	25%	-11%	5%	10%	-2%	5%	2	2	3	3	3
Exocrine pancreating insufficiency	Digestive enzyme preparations	12%	14%	11%	7%	6%	10%	9%	7%	10%	3%	3%	6%	10	12	12	12	12
Diabetes	Insulins, fast-acting	18%	23%	20%	13%	10%	17%	14%	3%	5%	-9%	-1%	2%	11	11	11	11	11
Diabetes	Insulins, intermediate- or long-acting combined with fast-acting	20%	22%	20%	14%	9%	17%	19%	7%	3%	-5%	0%	5%	11	11	11	11	11
Diabetes	Insulins, long-acting	21%	34%	16%	1%	1%	14%	24%	13%	-14%	-7%	-18%	-2%	4	4	4	4	7
Diabetes	Combinations of oral blood glucose lowering drugs	15%	16%	15%	9%	7%	12%	-1%	-1%	0%	-2%	-10%	-3%	8	11	11	15	21
Diabetes	Deipeptidyl peptidase 4 (DPP-4) inhibitors	15%	16%	15%	9%	7%	12%	1%	-3%	1%	-3%	-6%	-2%	6	6	6	6	6
Diabetes	Glucagon-like peptide-1 (GLP-1) analogues	12%	17%	14%	13%	10%	13%	3%	6%	9%	0%	7%	5%	3	4	4	8	9
Preventing or treating blood clots	Direct factor Xa inhibitors	13%	11%	12%	9%	9%	11%	0%	-4%	3%	5%	-2%	1%	3	3	5	5	8
Contraception	Progestogens & estrogens in combination	7%	12%	14%	12%	11%	11%	7%	12%	5%	2%	4%	6%	12	12	12	12	11
Male hypogonadism	3-oxoandrosten (4) derivatives androgens	11%	11%	17%	11%	10%	12%	-1%	14%	0%	11%	-4%	4%	9	9	9	9	9
Menopause	Estrogen treatment	24%	17%	20%	20%	13%	19%	18%	11%	11%	19%	9%	14%	21	20	20	20	20
Incontinence	Drugs for urinary frequency	12%	12%	15%	15%	11%	13%	9%	7%	4%	3%	-2%	4%	8	10	10	10	10
Hepatitis C	Direct-acting antivirals	17%	21%	0%	0%	0%	7%	12%	-65%	-30%	-23%	-12%	-29%	1	1	1	3	6
HIV	Combinations of direct-acting antivirals	7%	6%	6%	9%	7%	7%	8%	7%	7%	9%	3%	7%	3	4	4	5	6
Various	Selective serotonin (5HT1) agonists	10%	10%	14%	22%	18%	15%	14%	25%	3%	9%	1%	10%	12	12	12	12	12
Obstructive Airway Diseases	Selective beta-2-adrenoreceptor agonists	7%	7%	7%	10%	5%	7%	1%	10%	-3%	11%	-12%	1%	4	4	4	4	4
Obstructive Airway Diseases	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics	11%	9%	8%	8%	7%	8%	14%	-7%	-7%	-15%	-11%	-6%	10	10	10	10	10
Obstructive Airway Diseases	Glucocorticoids	9%	12%	7%	8%	7%	9%	7%	-5%	-5%	2%	-17%	-4%	11	12	13	13	13

Note: Inflation estimated using a Laspeyreys inflation index per equations (5) and (6) in the main text.

Exhibit 4: Growth in list and net prices per treatment course or annual treatment supply in select categories (2012-2017)



Year	2012	2013	2014	2015	2016	2017
Net Rebates (%)	39%	39%	47%	58%	63%	68%

Year	2012	2013	2014	2015	2016	2017
Net Rebates (%)	11%	18%	25%	28%	36%	38%

Year	2012	2013	2014	2015	2016	2017
Net Rebates (%)	29%	32%	4%	38%	50%	47%

Year	2012	2013	2014	2015	2016	2017
Net Rebates (%)	36%	34%	34%	32%	30%	29%

Notes: Insulins included are in ATC-level 4 categories A10AB (fast-acting), A10AD (fast-acting with intermediate or long-acting), or A10AE (long acting) and includes: apidra (2 formulations), basaglar, humalog / mix (3 formulations), humulin / mix (3 formulations), lantus (2 formulations), levemir (2 formulations), novolin (4 formulations), novolog / mix (3 formulations), soliqua, toujeo, tresiba (2 formulations), xultophy. The GLP-1 analogues category is identified by the ATC4 category A10BJ and includes: byetta, saxenda, tanzeum (2 formulations), trulicity (2 formulations), victoza. The HCV anti-virals category is identified by the ATC4 category J05AP and includes: daklinza (3 formulations), epclusa, harvoni, sovaldi, victrelis, viekira / xr, zepatier. The HIV anti-viral category is identified by the ATC4 category J05AR and includes: atripla, complera, descovy, genvoya, odefsey, stribild, triumeq, truvada.

Exhibit 5. Sources of Price Growth by Drug Category

Panel A: Decomposition of average price changes using list prices

	Avg price (000s)				Share of price growth explained by component (%)				
Category	2012	2017	Avg. annual change	Units	Within	Between	Cross	Entry	Exit
GLP-1 analogues for diabetes	3.26	8.82	1.11	Annual supply	63%	31%	1%	5%	0%
HCV anti-virals	31.93	81.22	9.86	Therapeutic course	27%	4%	-16%	84%	1%
HIV anti-viral combinations	17.60	26.90	1.86	Annual supply	81%	12%	-8%	16%	0%
Insulins	2.59	5.49	0.58	Annual supply	98%	1%	0%	2%	0%

Panel B: Decomposition of average price changes using net prices

	Avg price (000s)				Share of price growth explained by component (%)				
Category	2012	2017	Avg. annual change	Units	Within	Between	Cross	Entry	Exit
GLP-1 analogues for diabetes	2.91	5.47	0.51	Annual supply	44%	57%	-6%	5%	0%
HCV anti-virals	22.76	42.75	4.00	Therapeutic course	-282%	-9%	212%	176%	3%
HIV anti-viral combinations	11.29	19.17	1.58	Annual supply	59%	21%	-7%	26%	0%
Insulins	1.57	1.77	0.04	Annual supply	76%	7%	-16%	33%	0%

Note: Insulin, GLP-1 Analogues, HCV anti-virals, and HIV anti-virals are all defined as in Exhibit 4. Average price per annual supply or therapeutic course for each product-formulation is estimated using information in FDA labels. Prices for product-formulations are weighted according to market share to estimate an average price per annual supply ro therapeutic course for each drug category. Annual price growth estimates are decomposed into five components corresponding to distinct mechanisms contributing to spending growth. The w*ithin* term is the component of average price growth that is fully explained by growth in the prices for each product-formulation, assuming market share does not change. The b*etween, cross, entry, and exit* terms together comprise the component of average price growth attributable to market share increases among product-formulations with higher prices. The *between* term is the component of average price growth attributable to increasing market share among product-formulations that already had relatively high prices in the baseline year, The c*ross* term is the component of average price growth attributable to increasing market share among product-formulations with growing prices. The e*ntry* term is the component of average price growth attributable to the entry of relatively high price products in the endline year. Finally, the e*xit* term is the component of average price growth attributable to the exit of relatively low price products in the endline year. These terms are negative when the forces that they measure move in opposite directions to overall revenue growth. Equation (9) in the main text expresses this decomposition mathematically.

Exhibit 6: Sources of revenue growth

Panel A: Imputing revenue using list prices

	Drug spending ($B)					
	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017	Avg. Annual
Drug spending growth ($B)	11.0	24.7	27.3	12.5	16.1	18.3
Share explained by component						
Within	110%	63%	59%	109%	74%	76%
Between	-11%	-6%	-34%	-63%	-36%	-28%
Cross	-4%	-2%	-3%	-1%	2%	-2%
Entry	15%	45%	78%	55%	62%	55%
Exit	-10%	0%	0%	0%	-2%	-2%
Panel B: Imputing revenue using net prices						
Drug spending growth ($B)	6.2	13.0	7.8	2.2	4.5	6.7
Share explained by component						
Within	106%	30%	5%	7%	-12%	31%
Between	-5%	-2%	-84%	-167%	-41%	-38%
Cross	-8%	-5%	16%	42%	9%	4%
Entry	21%	77%	164%	219%	149%	106%
Exit	-15%	0%	0%	0%	-4%	-3%
Sample (N)	583	604	616	659	692	

Note: Drug spending growth based on data from 726 branded product-formulations sold in retail pharmacies for non-rare conditions. Samples differ by year due to product entry and exit. See text for further details on exclusions. Annual drug spending growth estimates are decomposed into five components corresponding to distinct mechanisms contributing to spending growth. The *within* term captures the annual growth in drug revenue explained exclusively by price increases in products available in both years, assuming quantities consumed do not change. The *between*, *cross*, *entry*, and *exit* terms therefore collectively capture the degree to which revenue growth is explained by changes in quantities. Specifically the *between* term captures the component of drug spending growth due to increases in quantity (volume) among products available in both periods (while prices are fixed). The *cross* term captures the component of revenue growth due to increases in the quantity for the product-formulations for which prices also increased. Finally, the *entry* term reflects gained revenue from new products and *exit* term reflects lost revenue from exiting products. The *within*, *between*, and *cross* terms may be positive or negative depending on whether they contribute or detract from growth in drug spending. These terms are negative when the forces that they measure move in opposite directions to overall revenue growth. Equation (10) in the main text expresses this decomposition mathematically.

Appendix

1. Assignment of drugs to Anatomical Therapeutic Classication (ATC) classes

ATC categories provide a 4-tiered classification system for each drugs, where each tier offers a different level of granularity; level-1 codes are the broadest while level-4 codes are the narrowest. We performed this mapping using a two-step process. First, we linked the National Drug Number (NDCs) associated with each product-formulation to ATC categories using RxNorm, an NIH provided tool that provides linkages between various drug identifiers. This procedure linked 64% to a single ATC-level 4 category, the narrowest level of classification. The remaining 36% of drug formulations where either linked to multiple ATC-level 4 codes (26%)[7] or were not linked to any ATC-level4 codes (10%) [8] by RxNorm.

In cases where RxNorm linked product-formulations to multiple or no ATC-level4 codes, we manually assigned the product-formulation to the most appropriate ATC-level 4 code based on the mechanism of action, FDA approved indication, and documentation from other government agencies such as the European Medicines Agency (EMA) and drug manufacturers where possible. We were unable to link only 20 (0.6%) of product-formulations.[9]

In cases where RxNorm linked to a single ATC code, we still manually reviewed each ATC code to assure an appropriate match. For 20 (0.6%) product-formulations, we manually modified the ATC code as it appeared RxNorm had an error. This typically occurred when the product was a combination product but RxNorm assigned it to the ATC-4 code for only one active ingredient.

[7]Drugs can erroneously link to multiple ATC-level4 codes for two main reasons. First, if the active ingredient in the drug appears in products for other indications, then the RxNorm may link the drug to each of the indications even if the brand was only approved for one. As an example, Protopic (tacrolimus) is approved for eczema whereas Prograf (tacrolimus) is approved for preventing rejection of organ transplants. However, because they both have tacrolimus as the active ingredient, they both were linked to ATC-level4 code D11AH (agents for dermatitis excluding corticosteroids) and L04AD (calcineurin immunosuppressants). Second, there are cases where a drug includes multiple ingredients. In many of these cases, there is an ATC code for the combination drug but RxNorm will return each ATC code individually. For example, Janumet (sitagliptin phosphate / metformin hcl) is a diabetes medication. There is an ATC4 code containing combination metformin HCL + sitagliptin phosphate (A10BD). However RxNorm will also return the code for metformin HCL (A10BD) and sitagliptin phosphate (A10BH) individually.

[8]Product-formulations can also erroneously fail to link to any ATC-level 4 code for multiple reasons. First, some drugs do not have an ATC code. In these cases we used the ATC-level 4 code of competitors with the same mechanism of action, when available. For example, Calquence (acalabrutinib) is a bruton tyrosine kinase (BTK) inhibitor for adults with mantle cell lymphoma. It does not have an ATC-level4 code but its main competitor Imbruvica (ibrutinib), also a BTK inhibitor, is assigned to the ATC4 code L01XE. Thus we manually assigned Calquence into L01XE. Second, some drugs actually do have an ATC code but the generic name associated with the NDC is listed in a slightly different way than in the ATC codebook, resulting in a failure to match. For example, the generic name for Seebri Neohaler is listed as glycopyrrolate in RxNorm and SSR. While there is no ATC code for glycopyrrolate per se, there is an ATC-level4 code for glycopyrronium bromide (R03BB). Glycopyrrolate is the active moiety of glycopyrronium bromide. Thus we manually linked Seebri Neohaler to R03BB.

[9]These included aurstat (2 formulations), biafine, hylatopic / plus (5 formulations), lacrisert, lodosyn, mugard, neutrasal, skelaxin (2 formulations), tetrix, theracys, tropazone (2 formulations), and zyflo / cr (2 formulations).

This approach to assigning drugs to ATC codes using a multitude of sources is similar to approaches used previously (Kesselheim et al., 2015).

2. Limitations of SSR data and Exclusions

We use data from SSR Health, LLC on list prices, net prices, revenue and unit sales. While these data provide the best available evidence on net prices to manufacturers by drug classes, the data do have important limitations. Most notably:

1. Symphony Health data on unit sales are measured with error - IQVIA and Symphony estimate unit sales from the subset of channels reporting to them. While data are relatively complete for drugs sold via traditional retail pharmacies, the coverage is less likely to be complete for products typically sold in non-traditional channels such as clinics, hospitals, and some specialty pharmacies. Underestimating sales for products sold in these channels can lead to overestimated net prices.

2. Discrepancies between when revenue and units sold are recorded – Manufacturers record revenue based on drug sales to wholesalers whereas IQVIA and Symphony record unit sales based on units dispensed at the pharmacy. Thus the transactions between wholesalers and pharmacies are mediated by inventories, and this can cause errors in net price estimates. This is most likely to be problematic for estimating net prices over narrow time bins. Moreover, at the time of product launch, product exit, or loss of exclusivity the lag between inventory and sales may be larger, exacerbating this type of error. This is because pharmacies are more likely to be building or depleting their inventory at this time.

3. Data on units per therapeutic course / annual supply– SSR Health, LLC provides estimates for units therapeutic course / annual supply only for select product-formulation combinations. These data are particularly likely to be incomplete for product-formulations with limited sales in recent years. This can make comparing prices and determining market share across drugs in certain categories more challenging.

4. Data do not capture generic sales – This feature limits the comprehensiveness of drug sales data for categories with high generic penetration.

5. Missing data – Companies do not always report drug sales in SEC filings and IQVIA and Symphony may also stop reporting drug sales. This may result in years where data on drugs is missing despite it being on the market.

Given these limitations, we limited our analysis to years and drug classes where the data were relatively reliable. For analyses requiring units per treatment course or annual supply, we

limited our analysis to classes where this data was available for several products.

Specifically, for our main analysis, we applied several exclusions. First, we restricted our analyses to products likely to be sold predominantly in retail pharmacies and for non-rare diseases, for which Symphony Health data are more complete. To do this, we applied several exclusions to exclude products likely distributed via clinics and hospitals. We first excluded all product-formulations where one or more formulations of the product-formulation had an injectable form according to SSR Health, LLC, with the exception of product-formulations that are typically self-administered (e.g., insulins). We excluded these product-formulations because a wide-array of injectable product-formulations are generally provided in clinics or hospitals, where IQVIA and Symphony are more likely to be inaccurate (e.g., botox, contrast material, etc.). We identified self-administered injectables exempt from this exclusion using published lists of self-administered product-formulations by the Centers for Medicare and Medicare Services (CMS). CMS maintains these lists to identify product-formulations excluded from coverage in physician offices or hospitals via Medicare Part B. The lists do not include all self-administered product-formulations, but includes products where CMS feels it necessary to clarify coverage. Thus it includes most injectable product-formulations that are self-administered.[10].

We excluded all other product-formulations for oncology, as these may be provided at a provider's office or hospital and thus have non-traditional distribution patterns. Indeed in Medicare, oral oncology product-formulations for which there is an infused version are typically covered by the physician (Part B) or hospital benefit (Part A) rather than Part D. We identified oncology products manually.[11] We also excluded inhaled vaccines, diagnostic products, and implantable product-formulations (e.g., Intra-uterine devices) as these would typically be provided at a provider's office. We similarly excluded iron chelating product-formulations, used to treat iron poisoning usually in an acute setting.[12]

We then excluded product-formulations for rare diseases as these are more likely to have specialty distribution channels and potentially be more subject to sampling error. To do this, we first excluded product-formulations classified for expanded exclusivity by the FDA as Orphan

[10]The lists can be found here: https://www.cms.gov/medicare-coverage-database/reports/sad-exclusion-list-report.aspx?bc=AQAAAAAAAAAA&

[11]The ATC-level2 code "L01" does include anti-tumor preparations. However other codes also include oncology treatments. For example, Provenge is a personalized immunotherapy for prostate cancer. It appears under the ATC-level2 code "L03" for immunostimulants. However this category also includes non-cancer treatments, such as old-generation treatments for hepatitus C.

[12]Vaccines were identified using the ATC-level2 code "J07". Diagnostic products were identified using the ATC-level2 codes "V09", "V08", "V04", and the ATC-level4 code "B05XA". Implantable drug formulations were identified using SSR Health¡ LLC data. Iron chelating product-formulations were identified using the ATC-level4 code "V03AC"

product-formulations. However, we did not exclude products that were only approved for an orphan indication via approval for a pediatric indication, as is suggestive that the product is actually more widely used. We also excluded product-formulations that were approved for diseases classifying as orphan indications, but did not receive orphan status presumably because they did not demonstrate clinical superiority. Specifically we excluded product-formulations approved for cystic fibrosis, pulmonary arterial hypertension, acromegaly, and multiple sclerosis. These were identified manually.

We then excluded several product-formulations due to missing or unreliable data. Specifically we excluded product-formulations that had missing data between 2012-2017 despite being on the market. We also excluded products facing loss of exclusivity within one year of baseline or endline as Symphony Health data are more likely to be inaccurate around this time. We excluded products that we could not assign to ATC codes. Finally, we excluded product-formulations that had an increase or decrease in list or net prices of over 5 standard deviations in one year between 2012-2017.

Our final sample included 726 branded product-formulations on the market in at least one year between 2012 and 2017. The number of product-formulations excluded at each step are provided in Appendix Exhibit 1. Summary statistics on the final sample can be found in Appendix Exhibit 2.

3. Sensitivity of rebate share analyses to alternative exclusions

We assessed the sensitivity of our main analysis of rebate share growth to alternative exclusions, with results illustrated in Appendix Exhibit 3. Overall, we find our results robust to alternative exclusion criteria.

4. Rebate share analysis by class

We performed the analysis of rebate share growth and price inflation by drug class on the 20 ATC-level 4 categories with the highest total sales revenue from 2012-2017 (Exhibit w). However, we excluded ATC-level 4 categories with 2 or fewer product-formulations offered across the study period. We also excluded poorly defined ATC-level 4 categories or ATC-level 4 categories, which include drugs that are not substitutes.[13]

[13]We excluded the following ATC-level 4 categories for being poorly defined or including poor substitutes: N03AX (other antiepileptics), N06AX (other anti-depressants), L04AX (other immunosupressants), J05AX (other antivirals), C10AX (other lipid modifying agents), C10BX (HMG CoA reductase inhibitors, other combinations), S01XA(other opthalmologics), N06DX (other anti-dementia drugs), A06AX (other drugs for constipation), A02BX (other drugs for peptic ulcer and gastrooesophageal reflux disease (GORD)), C09DX (angiotensin II receptor blockers (ARBs), C01EB (other cardiac preparations), N05AX (other antipsychotics), N02AX (other opioids),N07XX (other nervous system drugs), R03DX (Other systemic drugs for obstructive airway diseases), D10AX (Other anti-acne preparations for topical use), S01GX (Other antiallergics), D05AX (Other antipsoriatics for topical use), N05CM (Other hypnotics and sedatives), D11AX (Other dermatologicals), D01AE (Other antifungals for topical use),A10BX (Other blood glucose lowering drugs, excl. insulins), J01XX (Other antibacterials), D06AX (Other antibiotics for topical use), D06BX (Other chemotherapeutics for topical use), M03BX (Other centrally acting agents), J02AX (Other antimycotics for systemic use), N05BX (Other anxiolytics), G02CX (Other gynecologicals), A07XA (Other antidiarrheals), A11EX (Vitamin B-complex, other combinations), B03AE (Iron in other combinations), D07XA (Corticosteroids, weak, other combinations), R06AX (Other antihistamines for systemic use), J05AE (Protease inhibitors), L04AA (Selective immunosuppressants)

Appendix Exhibit 1. Sample exclusions

	Drug		2012 net revenue		2017 net revenue	
	N	Excluded	$B	% Excluded	$B	% Excluded
Panel A: Exclusions to identify drugs likely sold mostly in retail pharmacies						
Product-formulations on market between 2012-2017	**3020**		**192.7**		**268.7**	
Exclusions						
Exclusions to remove drugs likely administered in clinics or hospitals						
Injectable and not self-adminstered	620	20.5%	54.2	28.1%	86.8	32.3%
Oncology	142	4.7%	8.9	4.6%	23.6	8.8%
Inhaled vaccine	3	0.1%	0.8	0.4%	0.7	0.2%
Diagnostic compound	2	0.1%	0.1	0.0%	0.0	0.0%
Implant or device	8	0.3%	0.5	0.3%	1.0	0.4%
Exclusions to remove drugs likely sold via specialty distribution channels						
Orphan drug (except drugs only granted orphan status for a pediatric indication)	260	8.6%	22.8	11.8%	35.2	13.1%
Drug for a rare disease but not a designated orphan drug	23	0.8%	2.2	1.2%	8.0	3.0%
Product-formulations likely sold mostly in retail pharmacies	**1962**		**103.1**		**113.5**	
Panel B: Exclusions due to data limitations						
Product-formulations likely sold mostly in retail pharmacies	**1962**		**103.1**		**113.5**	
Exclusions						
Drug-formulation has missing data at some point between 2012-2017 despite drug being on market	1016	51.8%	16.0	15.5%	10.8	9.6%
Loss of exclusivity within one year of baseline or endline periods	188	9.6%	27.1	26.3%	9.1	8.0%
Not classified into an ATC category	5	0.3%	0.01	0.01%	0.002	0.002%
Drug is an outlier in net or list price change by > 5 std. dev. in at least 1 year	27	1.4%	0.7	0.7%	0.6	0.5%
Study sample	**726**		**59.3**		**92.9**	

Note: See Appendix Section 2 text for details on how exclusions were identified

Appendix Exhibit 2. Sample statistics

Therapeutic Area	2012				2017			
	Sample (N)	Revenue ($M)			Sample (N)	Revenue ($M)		
		Mean	SD	Total		Mean	SD	Total
Anti-infectives for systemic use	45	196	447	8,821	57	375	766	21,361
Antineoplastic and immunomodulating agents	20	273	573	5,460	29	383	731	11,095
Blood and blood-forming organs	6	46	52	278	10	590	830	5,901
Cardiovascular system	77	28	53	2,184	83	33	79	2,722
Dermatologicals	35	13	25	454	33	6	11	209
Hormonal preparations	19	82	150	1,552	20	149	323	2,978
Gastrointestinal tract & metabolism	99	195	406	19,340	147	179	354	26,335
Genito-urinary system & sex hormones	61	72	116	4,374	62	64	127	3,953
Musculo-skeletal system	16	148	398	2,376	17	37	76	633
Nervous system	137	48	129	6,588	176	59	127	10,448
Respiratory system	30	250	451	7,496	31	211	264	6,531
Sensory organs	16	23	38	369	16	45	69	719
Other	0	-	-	0	1	56	-	56
Total	**561**	**106**	**290**	**59,292**	**682**	**136**	**367**	**92,941**

Note: Therapeutic areas correspond to ATC level 1 classes. Sample refers to sample of product-formulations. The sample differs across years due to product entry and exit. Hormonal preparations category excludes sex hormones.

Appendix Exhibit 3. Sensitivity of rebate share growth analysis to exclusions

	Estimated rebate shares							Sample (N)					
	2012	2013	2014	2015	2016	2017	Avg. annual growth	2012	2013	2014	2015	2016	2017
Main result	**32%**	**33%**	**36%**	**43%**	**46%**	**48%**	**3.2 p.p.**	**561**	**571**	**589**	**614**	**654**	**682**
Sensitivity													
Remove all data quality exclusions	33%	34%	37%	43%	46%	48%	3.0 p.p.	1131	1181	1211	1172	1157	1087
Include drug-formulations with missing data at some point between 2012-2017 despite the drug being on the market	32%	34%	36%	42%	45%	48%	3.2 p.p.	759	814	847	843	890	851
Include drug-formulations undergoing loss of exclusivity within 1-year of baseline or endline	34%	34%	37%	42%	46%	48%	2.8 p.p.	736	746	770	795	835	862
Include drug-formulations with missing ATC codes	32%	33%	36%	43%	46%	48%	3.2 p.p.	564	576	594	619	657	685
Include drug-formulation with outlier changes of $>$ 5 s.d. list or net prices in any year	32%	33%	36%	43%	46%	49%	3.4 p.p.	585	596	614	640	679	707

Note: Sensitivity removing all data quality exclusions includes drug formulations with missing data between 2012-2017, loss of exclusivity within 1 year of endline or baseline, missing ATC codes, or outlier changes in list or net prices

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